REVISITING the ROLE of BETA-BLOCKERS in the MANAGEMENT of HYPERTENSION:

A CLOSER LOOK AT COMPLICATED CASES

ATLANTA, GEORGIA • DECEMBER 2, 2008
Session 5: Revisiting the Role of Beta-Blockers in the Management of Hypertension: A Closer Look at Complicated Cases

Learning Objectives

- Identify/discuss clinical considerations involved in the management of patients with complicated hypertension.
- Describe at least one of the latest clinical trial results on beta-blockers and its effects on metabolic parameters.

Faculty

Shawna D. Nesbitt, MD
Associate Professor, Department of Internal Medicine
University of Texas at Southwestern Medical Center at Dallas
Dallas, Texas

Shawna D. Nesbitt, MD, is associate professor of internal medicine at the University of Texas at Southwestern Medical Center at Dallas.

Dr Nesbitt received her medical degree from Hahnemann University School of Medicine, Philadelphia, Pennsylvania. She completed a medical internship and residency in internal medicine at Allegheny General Hospital, Pittsburgh, Pennsylvania. Dr Nesbitt completed her medical training with a fellowship in hypertension at the University of Michigan Medical Center, Ann Arbor.

Dr Nesbitt is a manuscript reviewer for American Journal of Hypertension, Ethnicity and Disease, Journal of the National Medical Association, and Hypertension. She has authored or coauthored more than 40 articles published in numerous peer-reviewed journals, including American Journal of Hypertension, Journal of Hypertension, and Journal of CardioMetabolic Syndrome. Dr Nesbitt has authored several chapters in books focusing on hypertension. She is a member of various professional societies including the Association of Black Cardiologists, American Society of Hypertension, and the International Society on Hypertension in Blacks.

Dr Nesbitt has given numerous international and national lectures with a focus on hypertension over the last 15 years.

Matthew J. Sorrentino, MD, FACC
Associate Professor of Medicine
University of Chicago Pritzker School of Medicine
Department of Medicine
Section of Cardiology
Chicago, Illinois

Matthew J. Sorrentino, MD, FACC, is associate professor of medicine at the University of Chicago Pritzker School of Medicine. Dr Sorrentino is a preventive cardiologist with clinical and research interests in hyperlipidemia and hypertension. He is an American Society of Hypertension hypertension specialist.

Dr Sorrentino received his medical degree from the University of Chicago Pritzker School of Medicine. He completed his internship and residency in Internal Medicine and a fellowship in Cardiovascular Disease at the University of Chicago Hospitals.

Dr Sorrentino is an abstract reviewer for the American College of Cardiology and the American Diabetes Association. He is a host on ReachMD, a satellite radio station for Medical Professionals. Dr Sorrentino has written numerous book chapters and over 70 articles published in journals such as The American Journal of Medicine, Journal of the American College of Cardiology and Journal of Geriatric Cardiology.

Faculty Financial Disclosure Statements

The presenting faculty reported the following:

Dr Nesbitt receives honoraria for serving as a consultant/speaker from Boehringer Ingelheim Pharmaceuticals, Inc.; Bristol-Myers Squibb; and Novartis Pharmaceuticals Corporations. Dr Nesbitt receives research support from AstraZeneca Pharmaceuticals LP and Pfizer Inc.
Dr Sorrentino receives speaking honoraria from Merck & Co., Inc.; Novartis Pharmaceuticals Corporation; Pfizer Inc.; and Takeda Pharmaceuticals Corporations.

**Education Partner Financial Disclosure Statements**
The content collaborators at The France Foundation have reported the following:

The content collaborators at The France Foundation have nothing to disclose.

**Drug List**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
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</thead>
<tbody>
<tr>
<td>acebutolol</td>
<td>Sectral</td>
</tr>
<tr>
<td>atenolol</td>
<td>Tenormin</td>
</tr>
<tr>
<td>bisoprolol</td>
<td>Zebeta</td>
</tr>
<tr>
<td>carvedilol</td>
<td>Coreg</td>
</tr>
<tr>
<td>labetalol</td>
<td>Normodyne, Trandate</td>
</tr>
<tr>
<td>lisinopril</td>
<td>Prinivil, Zestril</td>
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<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
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<tr>
<td>metoprolol</td>
<td>Lopressor, Toprol-XL</td>
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<tr>
<td>nebivolol</td>
<td>Bystolic</td>
</tr>
<tr>
<td>pindolol</td>
<td>Visken</td>
</tr>
<tr>
<td>propranolol</td>
<td>InnoPran-XL, Inderal</td>
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<tr>
<td>timolol</td>
<td>Betimol, Bloedren, Istalol</td>
</tr>
<tr>
<td>valsartan</td>
<td>Diovan</td>
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**Investigational**

- bucindolol
- celiprolol
- dilevalol

**Suggested Reading List**


Hypertension Progression with Age and Related Risk Factors

Shawna D. Nesbitt, MD
Associate Professor, Department of Internal Medicine
University of Texas at Southwestern Medical Center at Dallas
Dallas, Texas

Traditional CVD Risk Factors

- Family history
- Older age
- Male gender
- Smoking
- Physical inactivity
- Overweight/obesity
- Total-C/LDL-C/HDL-C/TG
- Hypertension
- Hyperglycemia


- Hypertension: SBP > 140, DBP > 90 mm Hg, or medicated for HT
- High cholesterol: > 240 mg/dl.
- Overweight: BMI > 25 kg/m²

Source: NHIS for smoking, ages > 18 and NHANES for the other risk factors, ages 35–74.

Ischemic Heart Disease Risk Increases with SBP, DBP, and Age


Synergistic Interaction of Traditional Multiple Risk Factors on CVD Risk

INTERHEART: Risk of AMI Associated With Risk Factors in the Overall Population

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>% Control</th>
<th>% Cases</th>
<th>OR (99% CI) Adj. for All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apo B/Apo A</td>
<td>20.0</td>
<td>33.5</td>
<td>3.25 (2.81, 3.76)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>26.8</td>
<td>45.2</td>
<td>2.87 (2.58, 3.19)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7.5</td>
<td>18.4</td>
<td>2.37 (2.07, 2.71)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21.9</td>
<td>39.0</td>
<td>1.91 (1.74, 2.10)</td>
</tr>
<tr>
<td>Abdominal obesity*</td>
<td>33.3</td>
<td>46.3</td>
<td>1.62 (1.45, 1.80)</td>
</tr>
</tbody>
</table>

**Protective Factor**

| Psychosocial        | —         | —       | 2.67 (2.11, 3.22)        |
| Vegetable/fruit daily| 42.4      | 35.8    | 0.70 (0.62, 0.79)        |
| Exercise            | 19.3      | 14.3    | 0.66 (0.76, 0.97)        |
| Alcohol intake      | 24.5      | 24.0    | 0.91 (0.82, 1.02)        |

*Upper limits of waist circumference.

Elevated BMI Increases the Risk of Cardiovascular Disease Mortality

Data are from 1 million men and women (average age, 57 years) followed for 16 years who never smoked and had no history of disease at enrollment.


Hypertension Is Associated With Insulin Resistance


Waist Circumference Correlates With BP and Insulin Resistance

EPIC-Norfolk Study: Every 1% Increase in HbA1c Increased CV Risk

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity</td>
<td>Waist*</td>
<td>39%</td>
</tr>
<tr>
<td>Men</td>
<td>&gt; 40 in</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>&gt; 35 in</td>
<td></td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>≥ 150</td>
<td>30%</td>
</tr>
<tr>
<td>Men</td>
<td>&lt; 40</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>&lt; 50</td>
<td></td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td>≥ 130/86</td>
<td>34%**</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>≥ 100 (NCEP ≥ 110)</td>
<td>13%**</td>
</tr>
</tbody>
</table>

*Lower cutpoints for Asian Americans.
**Or medication use

Diagnose by presence of 3 or more risk factors

AHA/NHLBI-Modified ATP III Criteria for Metabolic Syndrome

Metabolic Syndrome: Prevalence Increases With Age

47 million US adults (23%) have metabolic syndrome

Cardiovascular Disease Mortality and Metabolic Syndrome

Over Half of Patients Referred to Cardiologists Have Metabolic Syndrome

Inflammation in Metabolic Syndrome
Effects of Weight Loss* on Inflammatory Biomarkers

Baseline 12 months

ICAM = intercellular adhesion molecule; IL-6 = interleukin 6; TNF = tumor necrosis factor; VCAM=vascular cell adhesion molecule.


hsCRP Adds Prognostic Information to the ATP III Definition of Metabolic Syndrome

hsCRP < 3, No Metabolic Syndrome
hsCRP ≥ 3, No Metabolic Syndrome
hsCRP < 3, Yes Metabolic Syndrome
hsCRP ≥ 3, Yes Metabolic Syndrome

hsCRP = high-sensitivity CRP

Association of Insulin Resistance With Cardiovascular Risk Factors and Atherosclerosis

Obesity
Insulin resistance
Dyslipidemia
Hypertension
Endothelial dysfunction + ICAM-1
Inflammation + ↑CRP, ↑IL-6
Atherosclerosis


Summary

- The prevalence of obesity and diabetes is increasing
- Metabolic syndrome, a precursor to CVD and diabetes, is also on the rise
- Aggressive management of diabetes and other CVD risk factors is essential
- Primary care physicians are instrumental in addressing the therapeutic challenges faced by their patients with cardiometabolic risk factors
Evolution of Beta-Blockade and the Management of Complicated Hypertension

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Department of Medicine
Section of Cardiology
Chicago, Illinois

The Seventh Report of the Joint National Committee

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>Systolic BP (mm Hg)</th>
<th>Diastolic BP (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>and &lt; 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or 80–89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥ 160</td>
<td>or ≥ 100</td>
</tr>
</tbody>
</table>

Resistant hypertension is the failure to reach goal BP in patients who are adhering to full doses of an appropriate 3-drug regimen that includes a diuretic.


Percentage of Treated Patients With Hypertension at Goal 2003–2004

- Caucasians: 68%
- African-Americans: 52%
- Mexican-Americans: 57%
- Patients ≥ 60 years old: 44%
- Patients with diabetes: 25%


Awareness, Treatment, and Control of Hypertension in the US

Awareness: 49%
Treatment: 88%
Control: 57%
Control (Treated): 37%
Control (Treated, with diabetes): 37%
Control target for Healthy People 2000 (now 2010):

<table>
<thead>
<tr>
<th>Years</th>
<th>Control (All)</th>
<th>Control (Treated)</th>
<th>Control (Treated, with diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999-2000</td>
<td>35</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>2001-2002</td>
<td>35</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>2003-2004</td>
<td>35</td>
<td>17</td>
<td>14</td>
</tr>
</tbody>
</table>

*P* < 0.05 for the difference between 1999-2000 and 2003-2004.


Perceived Barriers to Optimizing β-Blocker Treatment

**Metabolic Concerns**
- Negative effects on lipid metabolism
- Negative effects on glucose metabolism
- Negative effects on renal blood flow
- Masked hypoglycemia

**Tolerability Concerns**
- Fatigue
- Impotence
- Weight increase
- Peripheral vasoconstriction (cold extremities)
- Depression

*Primarily in patients with hypertension and diabetes.


Evolution of Beta-Blockade

<table>
<thead>
<tr>
<th>First Generation</th>
<th>Second Generation</th>
<th>Third Generation</th>
<th>Next Generation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Selective</td>
<td>Selective</td>
<td>Vasodilating Non-Selective</td>
<td>Vasodilating Selective</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Atenolol, Metoprolol</td>
<td>Carvedilol, Labetalol</td>
<td>Nebivolol</td>
</tr>
</tbody>
</table>
**β-Blockers Are Heterogeneous**

<table>
<thead>
<tr>
<th>β-Blocker</th>
<th>ISA</th>
<th>Selectivity</th>
<th>Vasodilation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>+</td>
<td>Cardioselective</td>
<td>No</td>
<td>qid/bid</td>
</tr>
<tr>
<td>Atenolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>No</td>
<td>qid/bid</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>No</td>
<td>qd</td>
</tr>
<tr>
<td>Bucindolol</td>
<td>+</td>
<td>Nonselective</td>
<td>Likely via α1 blockade</td>
<td>bid</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>-</td>
<td>Nonselective</td>
<td>α1 blockade</td>
<td>qid/bid</td>
</tr>
<tr>
<td>Labetalol</td>
<td>+</td>
<td>Nonselective</td>
<td>No</td>
<td>bid</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>No</td>
<td>qd/bid</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>L-arginine/NO pathway</td>
<td>qd</td>
</tr>
<tr>
<td>Pindolol</td>
<td>++</td>
<td>Nonselective</td>
<td>No</td>
<td>bid</td>
</tr>
<tr>
<td>Propranolol</td>
<td>-</td>
<td>Nonselective</td>
<td>No</td>
<td>bid</td>
</tr>
<tr>
<td>Timolol</td>
<td>-</td>
<td>Nonselective</td>
<td>No</td>
<td>bid</td>
</tr>
</tbody>
</table>

ISA: intrinsic sympathomimetic activity


**Responses Mediated by β-Adrenergic Receptors in the Heart**

- **Beneficial effects**
  - Positive inotropic response: β1 > β2
  - Vasodilation: β1, β2

- **Harmful effects**
  - Myocyte apoptosis: β1
  - Myocyte damage/myopathy: β1 > β2 α1c
  - Fetal gene induction: β1

**The Vasodilating β-Blockers**

<table>
<thead>
<tr>
<th>Mechanisms</th>
<th>Agent(s)</th>
<th>Site of Activity</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>α1-receptor antagonism</td>
<td>carvedilol, acebutolol, bucindolol</td>
<td>receptors located in smooth muscle, heart</td>
<td>antagonism causes vasodilation</td>
</tr>
<tr>
<td>β2-agonism</td>
<td>dilevalol, celiprolol</td>
<td>receptors located in bronchi, blood vessels, gut</td>
<td>stimulation causes vasodilation</td>
</tr>
<tr>
<td>L-arginine/nitric oxide pathways</td>
<td>nebivolol, carvedilol</td>
<td>pathways located in blood vessel walls</td>
<td>stimulation causes release/activity of NO, and vasodilation</td>
</tr>
</tbody>
</table>


**Atenolol Increases the Risk of Stroke and All-Cause Mortality**

- Stroke: 1.26 (1.15-1.38)
- MI: 1.05 (0.91-1.21)
- All-cause mortality: 1.08 (1.02-1.14)

Favors Atenolol

**Non-Atenolol β-Blockers Do Not Increase Stroke, MI, or Mortality**

- Stroke: 1.20 (0.30-4.71)
- MI: 0.86 (0.67-1.11)
- All-cause mortality: 0.89 (0.70-1.12)

Favors Non-Atenolol β-Blockers

β-Blockers vs Diuretics: Elderly HTN

Clinical Outcomes With β-Blocker Therapy in Diabetes: UKPDS Study

GEMINI: Effect on Blood Pressure and Heart Rate

Change in Hemoglobin A1c GEMINI

Change in Insulin Resistance by Homeostasis Model Assessment (HOMA) GEMINI

Change in Glucose and Lipids in Patients With Diabetes
**Change in Insulin Sensitivity in Hypertensive Patients With Glucose Intolerance**

N = 25. Crossover; 16-week treatments. Nebivolol 2.5-5 mg and atenolol 50-100 mg daily.

*P < 0.05 vs placebo.

EH, euglycemic-hyperinsulinemic; IVGTT, intravenous glucose tolerance test.


**Effect of β-Blockade on Insulin Level and Sensitivity in Hypertensive Patients**

Effect of β-blockade on insulin level and sensitivity in hypertensive patients.

**Differing Effects of β-Blockers on Hemodynamics in Hypertensive Patients**

At 2 weeks.


**Nitric Oxide Is Vasoprotective and Anti-atherogenic**

Endothelial Dysfunction Predicts CV Events in Hypertensive Patients

Key Findings From Recent Lipid-Lowering Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Target BP (mm Hg)</th>
<th>Diabetic</th>
<th>CCB</th>
<th>Ideal</th>
<th>ASCOT-LA</th>
<th>ALLHAT-LT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALLHAT</td>
<td>SBP &lt; 140/DBP &lt; 90</td>
<td>9</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>ASCOT</td>
<td>140/90 (&lt; 130/80 DM)</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HOT</td>
<td>DBP &lt; 80</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UKPOD</td>
<td>DBP &lt; 85</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ARCD</td>
<td>DBP &lt; 75</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>INDNT</td>
<td>SBP &lt; 135/DBP &lt; 85</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MORD</td>
<td>MAP &lt; 92</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AASK</td>
<td>MAP &lt; 92</td>
<td>9</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

No. of antihypertensive agents

1 2 3 4

Key Findings From Recent BP-Lowering Trials

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<th>Target BP (mm Hg)</th>
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<td>0</td>
<td>1</td>
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<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
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<td>HOT</td>
<td>DBP &lt; 80</td>
<td>9</td>
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<td>0</td>
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<td>DBP &lt; 85</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
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<td>0</td>
<td>0</td>
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<td>9</td>
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<td>0</td>
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<td>0</td>
</tr>
</tbody>
</table>

No. of antihypertensive agents

1 2 3 4

Multiple Antihypertensive Agents Are Needed to Achieve Target BP

Drug | Incidence of Sexual Dysfunction (% of pts) | Source
--- | ----------------------------------------- | ---
Amlodipine Lisinopril | Desire (+18%)|Fantasies (+23%) | Fogari et al. Am J Hypertens. 2004;17:77.

This statistically significant difference in incidence of erectile dysfunction among various types of antihypertensive medications was demonstrated in women.

β-Blockers Associated with Sexual Dysfunction

JNC 7: Algorithm for Treatment of Hypertension

The Seventh Report of the Joint National Committee

<table>
<thead>
<tr>
<th>Compelling Indications</th>
<th>Diuretic</th>
<th>β</th>
<th>ACEI</th>
<th>ARB</th>
<th>CCB</th>
<th>AA</th>
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<tbody>
<tr>
<td>Heart failure</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>Post-MI</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>✔</td>
</tr>
<tr>
<td>High CAD risk</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td></td>
<td>✔</td>
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<tr>
<td>Diabetes</td>
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<td></td>
<td>✔</td>
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<td>✔</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
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<td>✔</td>
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<td>Recurrent stroke</td>
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</tbody>
</table>

AA: aldosterone antagonist; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; β, β-blocker; CCB, calcium channel blocker; MI, myocardial infarction; CAD, coronary artery disease.


Summary

• Some HTN studies and meta-analyses have shown inferior CV outcomes with β-blockers.
• The β-blockers are of critical importance in the management of patients with cardiovascular disease in general, and are useful in HTN.
• Vasodilating β-blockers (carvedilol, nebivolol) are associated with improved tolerability (metabolic symptoms) and have a better hemodynamic profile.
• Future trials of newer β-blockers may clarify their role in HTN.

Case Review for Complicated Hypertension

Case: 55-Year-Old Woman With Multiple CVD Risk Factors

New patient
• 55-year-old woman; smoker
• Previously diagnosed with slightly elevated BP, cholesterol, and glucose levels
  – Refused suggested medications
• States she is “a little overweight”
  – Asks to be prescribed weight loss pills
• Father died at age 62 of a heart attack
• Mother, age 74, developed diabetes in her mid-50s

Case: 55-Year-Old Woman With Multiple CVD Risk Factors

Physical exam
• Height: 5’5”
• Weight: 196 lb
• BMI: 32.6 kg/m²
• Waist: 44” (central obesity)
• BP: 160/96 mm Hg
• Pulse: 72 bpm
• Heart: RRR without murmur

Labs
• Total cholesterol: 238 mg/dL
• LDL-C: 105 mg/dL
• HDL-C: 32 mg/dL
• Triglycerides: 350 mg/dL
• Fasting glucose: 112 mg/dL
• HbA1C: 7.0
• Creatinine: 1.3 mg/dL
• Estimated GFR (MDRD): 62 mL/min/1.73 m²

RRR: Regular Rate and Rhythm; GFR: Glomerular Filtration Rate; MDRD: Modification of Diet in Renal Disease

ARS Question 1

Assuming lifestyle intervention has been implemented, which of the following CV risk factors need pharmacological treatment?

1. Blood Pressure
2. Triglycerides
3. Glucose
4. 1 & 3
5. All of the Above

AHA/NHLBI-Modified ATP III Criteria for Metabolic Syndrome

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Defining level</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal obesity</td>
<td>Waist circumference</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt; 40 in</td>
<td>44</td>
</tr>
<tr>
<td>Women</td>
<td>&gt; 35 in</td>
<td>350</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>≥ 150</td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt; 40</td>
<td>32</td>
</tr>
<tr>
<td>Women</td>
<td>&lt; 50</td>
<td>160/96</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>≥ 130/85</td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>≥ 100</td>
<td>112</td>
</tr>
</tbody>
</table>

Patient has all 5 risk factors

Case: 55-Year-Old Woman With Multiple CVD Risk Factors

**Diagnosis:**
- Hypertension with metabolic syndrome
- Dyslipidemia
- Smoker

Patient is identified as being at moderate risk for a CV event by Framingham risk score (17% 10-year risk)

ARS Question 2

In addition to low dose aspirin, she agrees to take a “couple” of pills; which of these would be most useful?

1. RAS blocker/calcium antagonist
2. Calcium antagonist with a statin plus fixed dose of a RAS blocker/diuretic
3. RAS blocker/β-blocker plus fenofibrate
4. RAS blocker/calcium antagonist plus fenofibrate
5. RAS blocker/calcium antagonist plus niacin

Case: 50-Year-Old Man With T2DM and CAD

- 50-year-old man
- Being seen for increased triglycerides refractory to fibrates
- Past medical history:
  - Diagnosed with T2DM at age 42
  - 5 vessel CAD with CABG at age 47
- Family history:
  - Father died at age 62 with CAD
  - Paternal grandfather died at age 65 with CAD
  - Mother and maternal grandmother with T2DM

Medications
- ASA/Warfarin
- Metformin 1000 BID
- Glyburide 2.5 BID
- Fenofibrate 145 mg/day
- Metoprolol 100 mg/day
- HCTZ/triamterene 25/100 mg/d
- Niacin (intermittent/noncompliant)
- Fish oil x 2 grams/day
- Multivitamin x 1 daily

Case: 50-Year-Old Man With T2DM and CAD

- Physical exam
  - 220 lbs and 71 in = BMI 30.7 kg/m²
  - Central obesity
  - CABG scars
  - BP: 138/86 mm Hg
  - P: 56 regular

Case: 50-Year-Old Man With Type 2 DM and CAD

<table>
<thead>
<tr>
<th>Lab</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose</td>
<td>146 mg/dL</td>
<td>&lt; 100 mg/dL</td>
</tr>
<tr>
<td>HbA1c</td>
<td>7.8%</td>
<td>5% (T2DM goal &lt; 7%)</td>
</tr>
<tr>
<td>ALT</td>
<td>66 IU/L</td>
<td>≤ 60</td>
</tr>
<tr>
<td>hsCRP</td>
<td>1.6 mg/L</td>
<td>&lt; 2.0</td>
</tr>
<tr>
<td>Insulin</td>
<td>28.1 uU/mL</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Trig</td>
<td>289 mg/dL</td>
<td>&lt; 150</td>
</tr>
<tr>
<td>LDL-C</td>
<td>117 mg/dL</td>
<td>&lt; 130</td>
</tr>
<tr>
<td>HDL-C</td>
<td>29.9 mg/dL</td>
<td>≥ 40</td>
</tr>
</tbody>
</table>
ARS Question 3

How should the meds/lifestyle be adjusted?

1. Taper the metoprolol and diuretics and substitute a vasodilating beta blocker and ACE inhibitor for BP
2. Stop fenofibrate and start (titrate) sustained-release niacin 2.5 g at bedtime
3. Low carbohydrate diet/increase exercise
4. Increase glyburide to 5 mg BID
5. All of the above

Case: 50-Year-Old Man With T2DM and CAD: Teaching Points

Multiple cardiovascular risk factors

– s/p CABG (secondary prevention)
– Dyslipidemia (Trig/HDL-C)
– Obesity (BMI > 27 with comorbidities)
– Diabetes